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Etiologic evaluation of male patients diagnosed with anemia in the first consultation of the hematology department

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ABSTRACT

Aims: Anemia is a decrease in hemoglobin (Hb) levels below the normal values determined by gender. Since anemia is a laboratory finding, its etiology must be investigated. The present study aimed to investigate the etiologic spectrum of male patients diagnosed with anemia in the first consultation of a tertiary hospital hematology department.

Methods: This study was conducted with male patients who were consulted at İnönü University, Turgut Özal Medical Center, Adult Hematology Department between the dates of 2010-2015. Adult male patients aged 18 years and older, who were diagnosed with anemia in the first consultation were included in the study. Hb levels under 13 g/dl in the complete blood count were accepted as anemia criteria. The study was carried out retrospectively by examining the records of the hospital automation system.

Results: The records of a total number of 7840 adult male patients were examined and 473 (6%) of them were found to have anemia when they first consulted in the hematology department. Iron deficiency was the most common etiological cause with the number of 97 patients (20.5%). In the first consultation; malign diseases were found in 50.3% (238), and benign diseases were found in 49.7% (235) of the patients, as the etiologic causes of the anemia. Multiple myeloma (MM) was found to be the most common malignant disease with a rate of 26.5% (63 patients), and isolated iron deficiency was found to be the most common benign disease with a rate of 41.3 % (97 patients); among the etiologic factors or anemia.

Conclusion: In our study, malignant diseases were detected as the etiological cause in more than half of the adult male patients with anemia in their first consultation. We think that it is important to keep this situation in mind in the etiology of anemias, especially considering the profile of patients referred to tertiary hospitals.

Keywords: Anemia, etiology, male

INTRODUCTION

Anemia is defined as a decrease in hemoglobin (Hb) levels below the normal values determined considering age and gender. According to World Health Organization (WHO)'s criteria; Hb levels, less than 12 g/dl in women, less than 13 g/dl in men, and less than 11 g/dl in pregnant women are defined as anemia.[1] Anemia is a laboratory finding that is seen in the diagnosis and/or follow-up of many diseases. Therefore, the etiological cause must be investigated in patients with anemia in clinical practice. There are two general approaches; (I) kinetic and (II) morphological in defining the causes of anemia. Classification is made according to the mechanisms causing anemia in the kinetic approach (erythrocyte production deficiency, increase in erythrocyte destruction and blood loss), and according to the mean erythrocyte volume (microcytic, normocytic, macrocytic) in the morphological approach.[2] Iron deficiency anemia (IDA) due to iron deficiency is the most common type of anemia worldwide and is estimated to be approximately 50% of all anemia.[3] Especially children and women of childbearing age are more at risk for RIA. However, the differential diagnosis of anemia due to many etiological causes besides iron deficiency in adult men and postmenopausal women may be an important problem.

Anemia may be the first laboratory finding in some malignancies. The incidence of anemia varies on the histological type and stage of the malignancy, as well as the duration of diagnosis and treatment procedures. The etiology of anemia that occurs due to malignancies, is often multifactorial. As known; the frequency of IDA is lower in adult men than in children and women of childbearing age. For this reason, in adult males with anemia, many other etiological causes, including malignant diseases, should be considered besides iron deficiency. The number of studies investigating the etiological causes of anemia in our country is relatively small and data on the prevalence of anemia is limited. This study;

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it was aimed to investigate the etiological spectrum of male patients diagnosed with anemia in the first consultation of the hematology department.

METHODS

The study was conducted with the permission of İnönü University Scientific Researches and Publication Ethics Committee (Date: 26.10.2016, Decision No: 2016/15-1). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was conducted with adult male patients diagnosed with anemia at the first admission to the adult hematology outpatient clinic. A total of 7840 adult male patients who applied to the adult hematology outpatient clinic of İnönü University, Turgut Özal Medical Center between January 2010 and December 2015 were included in the study. The Hb values below 13 g/dl in the complete blood count were considered as anemia, and patients at the age of 18 and above were considered as adults. In this retrospective study, anemia was detected in the first admission, in 473 (6%) of 7840 adult male patients whose medical records were examined. In our study, the etiological causes of anemia that were detected at the first admission of 473 patients, were evaluated from the hospital automation system records. Patients with compatible peripheral smear data and ferritin levels below 15 ng/ml were diagnosed with RIA, and patients with vitamin B12 levels below 200 pg/ml were diagnosed with megaloblastic anemia due to vitamin B12 deficiency. Increased Hb A2 levels (≥3.5%) in Hb electrophoresis with anemia were accepted as beta thalassemia minor. The presence of pancytopenia in complete blood count and hypocellular bone marrow without abnormal infiltration and reticulin fiber increase were aplastic anemia (AA) criteria. Patients with low thrombocyte levels accompanying anemia were diagnosed with primer immune thrombocytopenia (ITP) after eliminating external factors that can cause thrombocytopenia. Spherocytic and polychromatic erythrocytes in the peripheral smear, increased serum indirect bilirubin/lactate dehydrogenase levels and direct Coombs test positivity were criteria for autoimmune hemolytic anemia (OIHA) diagnosis. Increased schistocyte (≥1%) rates in peripheral smear and Coombs test negativity with anemia were criteria for microangiopathic hemolytic anemia (MAHA) diagnosis.

Among the malign diseases, patients with increased clonal plasmacytoma (≥10%) in bone marrow were diagnosed with multiple myeloma (MM). Patients with the presence of blasts in peripheral smear and/or bone marrow inspection were diagnosed with acute myeloblastic leukemia (AML) and/or acute lymphoblastic leukemia (ALL) as a result of flow cytometry and cytogenetic research. Increased leukocyte count in complete blood count, specific peripheral smear findings and Philadelphia chromosome presence in cytogenetic analysis were accepted as chronic myeloid leukemia (CML) criteria. Chronic lymphocytic leukemia (CLL) was diagnosed with an increase of monoclonal B lymphocytes in peripheral blood (≥5.000%/microL) that have special phenotypic characteristics for KLL in flow cytometry. Non-Hodgkin lymphoma and Hodgkin lymphoma (HL) diagnoses were given histopathologically after lymph node and/or organ biopsy. Myelodysplastic syndrome (MDS) and primer myelofibrosis (PMF) diagnoses were given according to the diagnostic criteria of the World Health Organization.[4,5] Diagnosis of solid tumors was made by the relevant organ/tissue biopsy. Patients; who did not continue their follow-ups for advanced examination, did not approve interventional procedures were diagnosed with anemia and received medical treatment before the study, were excluded from the study. In addition, anemias due to non-hematological diseases (infection, rheumatological, kidney diseases, etc.) were not included in the study.

Statistical Analysis

Statistical evaluation of data was done using SPSS for Windows Version 17.0 software. Identification of quantitative data of the variants was presented as mean±standard deviation (SD); identification of qualitative data was presented as number and percent (%). With the Kolmogorov-Smirnov test; Hb, WBC and trombocyte levels were not normally distributed according to benign and malign causes ($p>0.05$). So comparison of benign and malign causes was made by using the Whitney-U test. Values of $p<0.05$ were considered statistically significant.

RESULTS

A total of 473 adult male patients diagnosed with anemia at the first visit were included in to study. The etiological causes of anemias were evaluated under two main titles benign and malignant diseases. It was detected that anemia was developed in 238 (50.3%) of 473 patients due to malignant etiological causes and 235 (49.7%) due to benign etiological causes. MM was the most common etiological cause with 63 (26.5%) patients, while AML was the second with 39 (16.4%) patients and CLL was the third with 32 patients (13.4%). IDA was the most common cause of anemia with 97 (41.3%) patients with benign etiologies. The second common benign cause was IDA+vitamine B12 deficiency with 60 (25.5%) patients and the third common benign cause was isolated vitamine B12 deficiency with 37 (15.8%) patients. IDA was also the most common cause among the total of benign and malign etiologies with 97 (20.5%) patients.

Table shows all etiological causes of anemia and their percentages in 473 patients who participated in this study:

Table. Etiologic causes of anemies

Etiology	n of p	%
Iron deficiency anemia	97	20.5
Multiple myeloma	63	13.3
Iron deficiency+vitamine B12 deficiency	60	12.7
Acute myeloid leukemia	39	8.2
Vitamine B12 deficiency	37	7.9
Chronic lymphocytic leukemia	32	6.8
Chronic myeloid leukemia	28	5.9
Beta thalessemia minor	26	5.5
Non-Hodgkin lymphoma	25	5.3
Myelodysplastic syndrome	18	3.8
Acute lymphoblastic leukemia	16	3.4
Aplastic anemia	8	1.7
Hodgkin lymphoma	7	1.5
Primer myelofibrosis	6	1.3
Solid tumor	4	0.8
Primer immune thrombocytopenia	3	0.6
Hemolytic anemia	3	0.6
Thrombotic thrombocytopenic purpura	1	0.2
Total	**473**	**100.0**

The average age of the patients included in the study was 59.9 (20-90) years. While the average age in patients with benign etiologies was 55.6 years, the average age in patients with malign etiologies was 64.3 years. The mean Hb value of 235 patients with benign etiology was 9.57±2.109 g/dl, the mean white blood cell (WBC) was 6.490±2.842/µL and the mean platelet count was 260.430±129.069/µL, while the mean Hb value of 238 patients with malignant etiology was 9.66±2.195g/dl, the mean WBC was 26.652±43.146/µL and the mean platelet count was 218.160±273.276/µL. While there was no statistical difference in Hb values between benign and malignant causes (p=0.492), there was a significant difference in terms of leukocyte and platelet counts (p=0.0001).

DISCUSSION

Anemia is a global health problem due to its high prevalence and the associated significant morbidity and mortality in the adult population. Anemia can be seen in all periods of life, it is more common in pregnant women and young children. In a WHO report published in 2011, the global anemia prevalence was estimated to be 38% in pregnant women, 29% in non-pregnant women and 43% in children.[6] Data on the prevalence of anemia in our country is relatively limited. Çoban et al.[7] investigated the frequency of anemia in 2100 patients aged 65 years or older who applied to the internal medicine outpatient clinic. The frequency of anemia was reported as 30.5% in this study population in which anemia frequency was not reported by gender. Şahin et al.[8] studied a total of 521 (48% male and 52% female) patients 65 years and older, they reported that 63% of the patients were anemic, and the frequency of anemia in male (69.1%) patients was significantly higher than female (57.7%) patients. In a larger study conducted by Memişoğulları et al.[9] including 2187 adults (18-92 years of age) and involving the etiology and prevalence of anemias in the Turkish population, it was reported that 565 (25.8%) patients were anemic, and the prevalence of anemia was 30.0% in women and 18.2% in men. The prevalence of anemia was observed as 16% in another study of 66 male patients over the age of 65.[10]

In the present study, anemia rates were determined as 6.0% among adult male patients at the first consultation in the hematology department. In these studies reported by different centers in our country, it seems that the results of the prevalence of anemia are contradictory. This may be due to the different parameters such as the number of patients, gender, socio-economic conditions, geographical regions and age in these studies. In addition, besides anemia due to non-hematological diseases (infection, rheumatological, kidney diseases, etc.) were not included in the study, we think that such factors may play a role in the lower prevalence of anemia in our study, compared to other studies; (I) only male patients were included in our study, (II) and the study was conducted in the tertiary health institution. However, Çetin et al.[11] investigated the prevalence of anemia in a total of 1095 adults over 18 years of age in the Tokat region, they reported the frequency of anemia as 15.9% in women, whereas 6.1 % in men, at a rate similar to our results.

The most common type of anemia worldwide is IDA, with a rate of 50% among all anemia types.[11] IDA is also the most common cause of anemia due to nutritional deficiencies. Although our study was conducted in a tertiary hospital, we found iron deficiency as the most common cause of anemia in male patients who applied to the adult hematology outpatient clinic in the literature. The incidence of IDA varies depending on different age groups, gender and socio-economic conditions. Although IDA occurs in all age groups, it is most common in children, pregnant women and women of childbearing age. The incidence of IDA in developed countries is reported as 2-5% in adult men and postmenopausal women, 10% in women aged between 15-59, and 23% in pregnant women.[12] In our study we investigated the etiologies of anemia, we detected anemia due to isolated iron deficiency in 97 of 473 male patients (20.5%). Sezer et al.[14] studied 546 anemia patients aged 65 and over in Izmir, they reported that 29.9% (163 patients) of patients were diagnosed with IDA and 79 of them (48.5%) were male. In another study, Dilek et al.[15] investigated IDA prevalence among 642 (168 male, 474 female) adults in Van region, they reported IDA rates as 15.9% (17.3% among females and 11.9% among males). In these reported studies, the inconsistency in IDA rates with our results may be related to the characteristics of the groups in which the study was conducted, as well as the number and age of samples. As it is known, chronic gastrointestinal system hemorrhages due to various diseases in elderly patients are the main cause of IDA.

Megaloblastic anemia caused by vitamin B12 deficiency is one of the most important nutritional anemias. In our study, 37 (7.9%) of the patients diagnosed with anemia in their first admission were categorized as megaloblastic anemia due to isolated vitamin B12 deficiency. An important study conducted in the USA that examined the etiological causes of anemia among 60-year-old and older patients reported that vitamin B12 deficiency was the cause of 17.2% of nutritional anemia and 5.9% of all anemia types.[15] Also in this study, iron deficiency+folate deficiency and vitamin B12 deficiency+iron deficiency are reported to constitute 9.9% of nutritional anemia and 3.4% of all anemia types. Memişoğulları et al.[9] reported a 29.3 % prevalence of vitamin B12 deficiency, among 565 adult patients with anemia. In another study, Karakuş et al.[17] investigated the etiology of 561 anemia patients at the university hospital adult hematology department, they determined the frequency of vitamin B12 deficiency-related anemia as 7.6%. In addition, in this study, the researchers reported iron and vitamin B12 deficiency as an etiological cause in 43.8% of patients with anemia. In this study, we found vitamin B12 deficiency anemia together with DEA in 12.7% (60 patients) of our patients with anemia. In these types of anemias called combined nutritional anemias, sometimes more causes of anemia (DEA and vitamin B12 deficiency and folate deficiency) can be detected simultaneously. In another study reported from abroad that included a total of 424 hospitalized patients aged 65 and over, vitamin B12 deficiency anemia was reported to be much lower (3.8%).[18]

Anemia may be the first and/or only sign of malignancies such as MDS, hairy cell leukemia and GIS adenocarcinoma. Anemias are one of the most important hematological findings in malignant patients. It was reported that more than 30% of malignant patients had anemia associated with malignancy at the time of diagnosis, and in a large series, more than half (63%) of the patients were anemic at the time of diagnosis.[19,20] The pathogenesis of anemias associated with hematological malignancies or solid tumors is multifactorial. In patients with malignancies; anemia occurs due to one or more of the disorders including; functional iron deficiency, bone marrow infiltration, pure erythroid array aplasia, hemolysis, malnutrition, microangiopathy, hemophagocytosis, cytokine-

induced erythropoiesis inhibition, and trombocytopenic hemorrhage (mucocutaneous and/or GIS bleeding). In our study, we demonstrated that anemia was due to malignant diseases in 50.3% (238 patients) of the 473 male patients diagnosed with anemia on their first admission to adult hematology outpatient clinic. MM was the most common etiologic cause with a rate of 26.5% (63 patients) among these 238 patients. MM patients were followed by AML (16.4%) and CLL (13.4%) patients, respectively. We think that the main reason for the rate of malignant patients to be more than 50% in the etiology of anemia is related to our patient population who applied to our hematology outpatient clinic. The majority of these patients were referred to our clinics because of hematological anomalies detected in primary or secondary health institutions.

CONCLUSION

As a result; studies investigating the causes of anemia in the adult age group in our country are still insufficient. In this study, we aimed to investigate the etiological causes of male patients diagnosed with anemia for the first time in the adult hematology outpatient clinic. 474 male patients we included in our study, we detected malignant diseases in 50.3% and benign diseases in 49.7% of them as the etiological cause of anemia. The relatively low number of patients, exclusion of chronic disease anemia and the inclusion of only adult male patients limit the value of our study. Further studies are needed on this subject.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of İnönü University Scientific Researches and Publication Ethics Committee (Date: 26.10.2016, Decision No: 2016/15-1).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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